بسم الله الرحمن الرحيم

Antiphospholipid Syndrome

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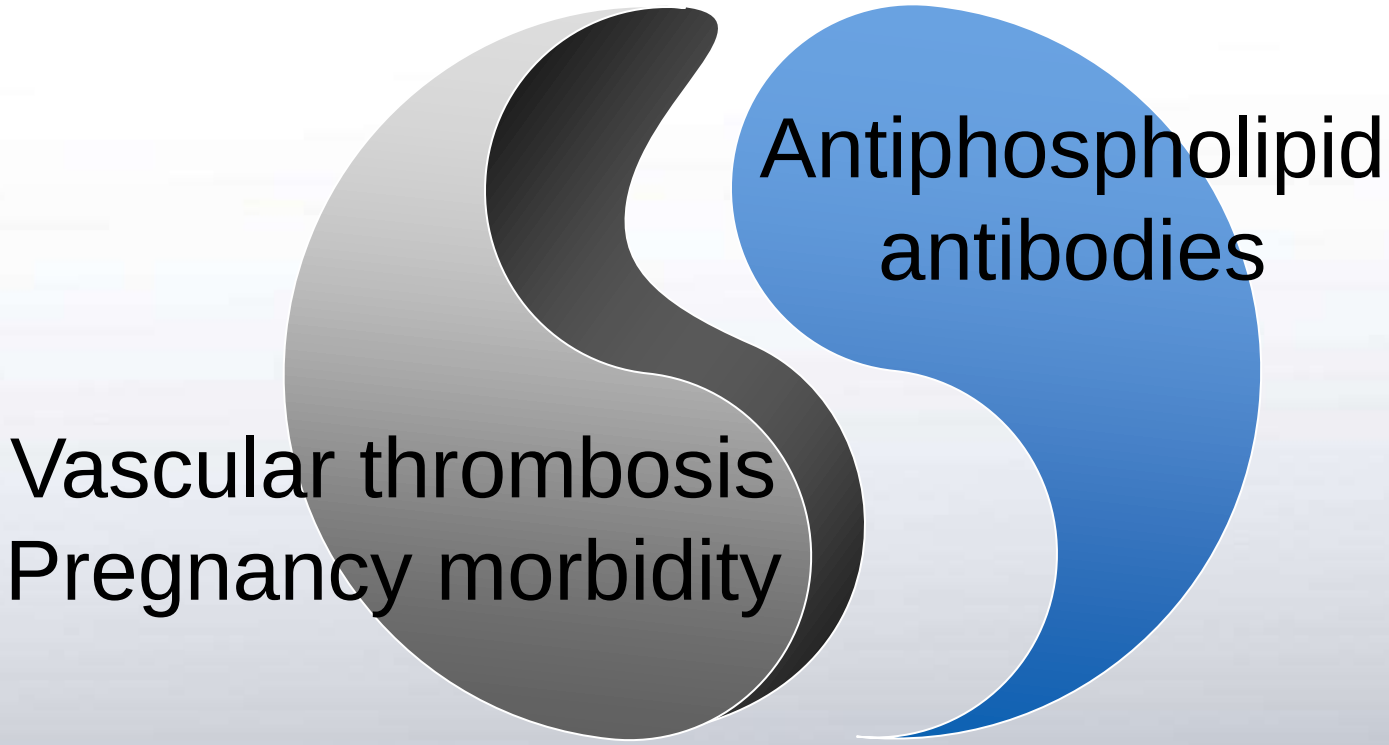
Rheumatology and Immunology

Autoimmune disorder



Why should we make the diagnosis?

Epidemiology

- antibodies (low, transient) 5-10% in healthy population
- Significant titer in < 1%
- 4% have annual risk of thrombosis
- Up to 40% SLE patients
- 20% RA patients

- 29% young stroke patients
- 15% recurrent miscarriage
- 15-20% deep vein thrombosis
- 50% mortality in catastrophic APS
- female : male = 2 : 1

Table 1. Diseases with aPL

SYSTEMIC ATUTOIMMUNE DISEASES
- Systemic lupus erythematosus
- Rheumatoid arthritis
- Systemic sclerosis
- Primary Sjögren's syndrome
- Dermato- and polymyositis
- Psoriatic arthropathy
- Vasculitis
  - Polyarteritis nodosa/microscopic polyarteritis
  - Giant cell arteritis
  - Behçet's disease
  - Relapsing polychondritis
  - Leucocytoclastic vasculitis
  - Mesenteric inflammatory veno-occlusive disease
  - Capillaritis
  - Other vasculitis

INFECTIONS
- Viral
  - HIV infection
  - Mononucleosis
  - Rubella
  - Parvovirus
  - Hepatitis A, B, C
  - Mumps
- Bacterial
  - Syphilis
  - Lyme disease
  - Tuberculosis
  - Leprosy
  - Infective endocarditis
  - Rheumatic fever
  - *Klebsiella*
- Protozoal
  - Malaria
  - Toxoplasmosis

MALIGNANCIES

Solid tumors
- Lung
- Colon/Caecum
- Cervix
- Prostate
- Liver
- Kidney (hypernephroma)
- Thymus (thymoma)
- Maxilla
- Ovary
- Breast

Hematologic
- Myeloid and lymphatic leukemias
- Polycythemia vera
- Myelofibrosis

Lymphoproliferative diseases
- Hodgkin's disease
- Non-Hodgkin's lymphoma
- Lymphosarcoma
- Cutaneous T-cell lymphoma/Sézary syndrome

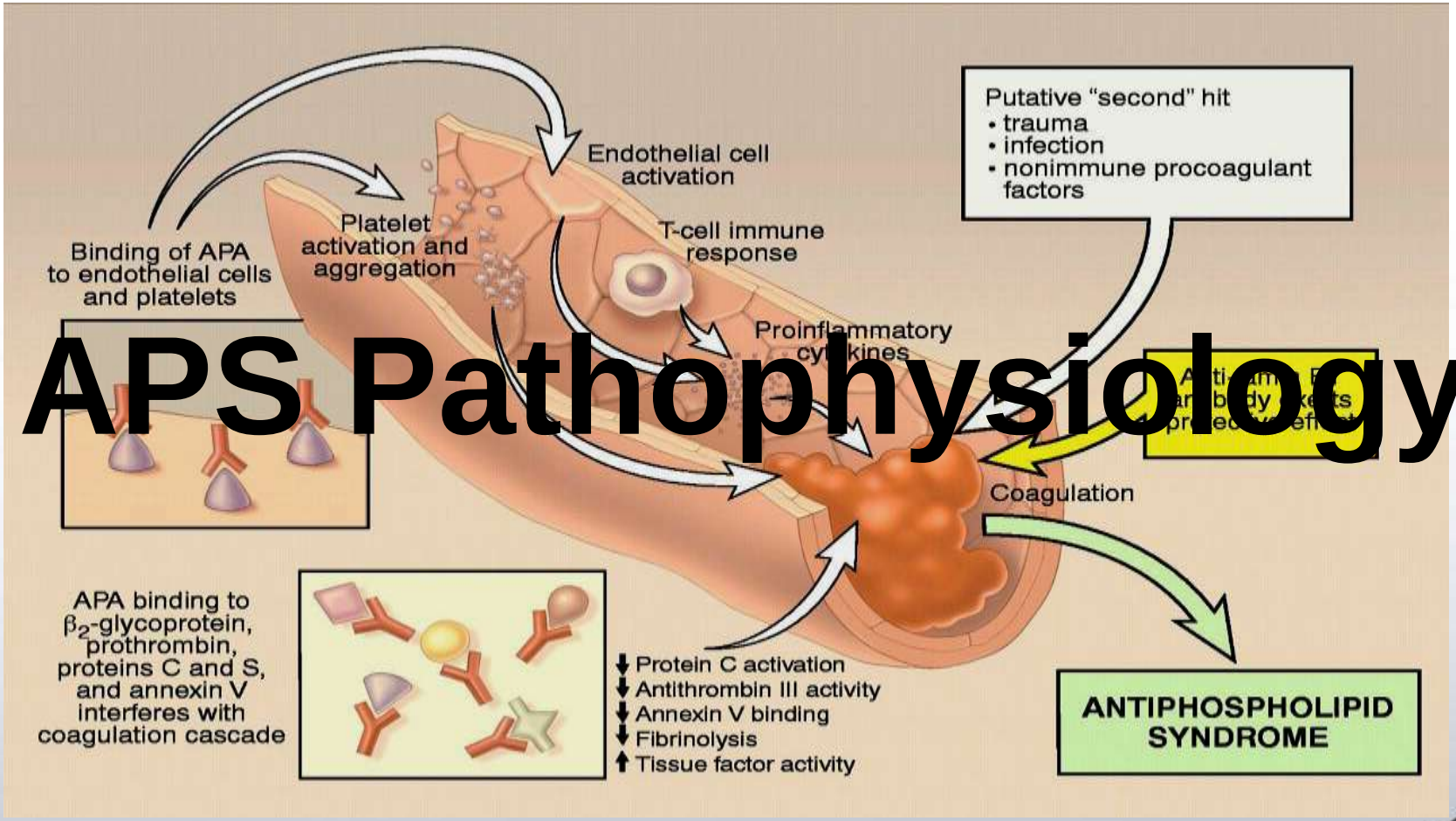
Paraproteinemias
- Monoclonal gammapathies
- Waldenström macroglobulinemia
- Myeloma

NON-MALIGNANT HEMATOLOGIC CONDITIONS
- Idiopathic thrombocytopenic purpura
- Sickle cell disease
- Pernicious anemia

DRUGS
- Procainamide
- Phenothiazines
- Ethosuximide
- Chlorothiazide
- Quinine
- Oral contraceptives

OTHER CONDITIONS
- Diabetes mellitus
- Autoimmune thyroid disease
- Inflammatory bowel diseases
- Dialysis
- Klinefelter's syndrome

APS Pathophysiology



Journal of Thrombosis and Haemostasis, **4**: 295–306

SPECIAL ARTICLE

International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS)

diagnosis

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for APS. Members of the workshop panel included all of the

Clinical Criteria

- **Vas**

el,

in

by

obj

Pregnancy morbidity:

- ≥3 consecutive miscarriages (<10 weeks' gestation)
- ≥1 fetal death (>10 weeks' gestation with normal fetal morphology)
- ≥1 premature birth (<34 weeks' gestation with normal fetal morphology) due to pre-eclampsia or severe placental insufficiency

Laboratory criteria

- **Lupus anticoagulant**,
- **Anticardiolipin antibodies** (ACA), IgG or IgM .
- **Anti-beta-2-glycoprotein I antibodies** (anti-B2GPI), IgG or IgM

present on at least 2 occasions

12 weeks apart

titer> 40 GPL, MPL

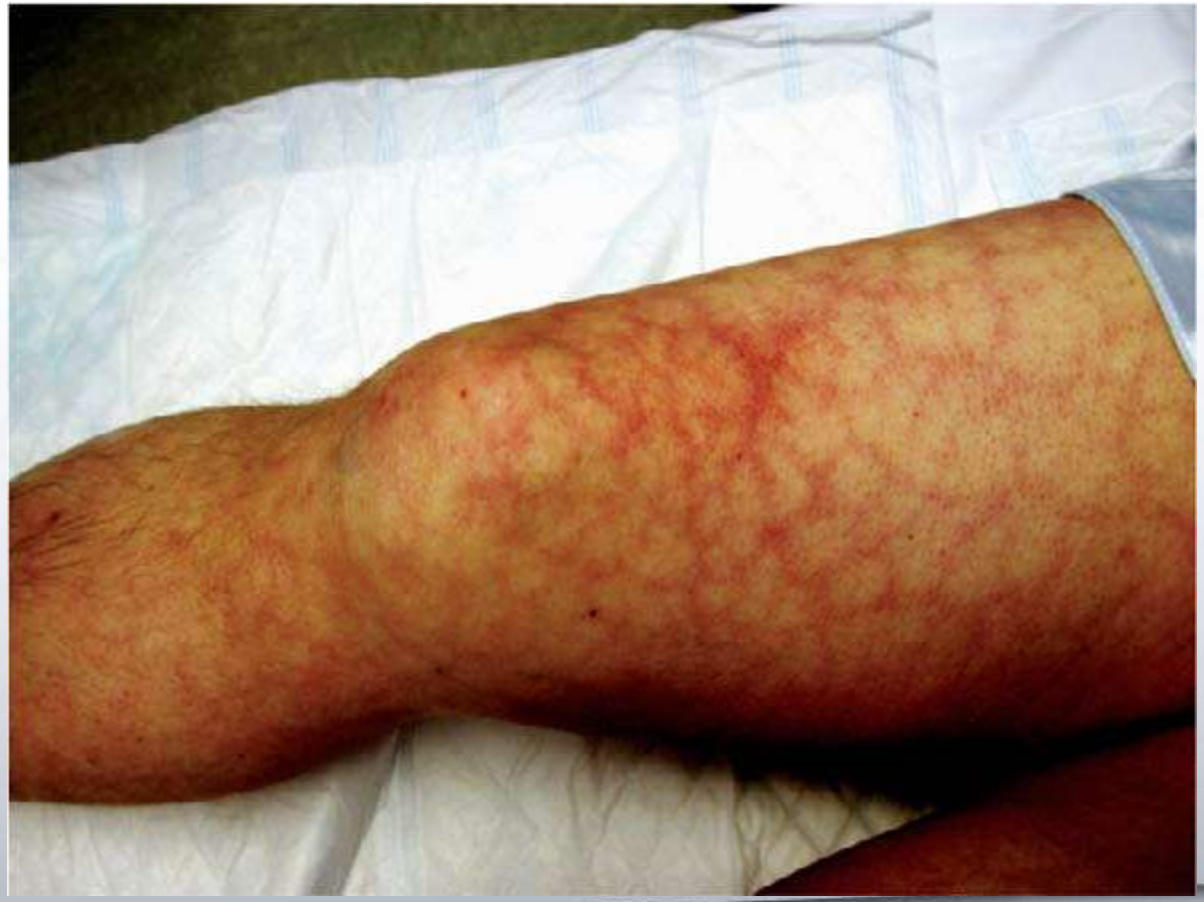
A diagnosis of APS should not be made if a period of <12 weeks or > five years separates the clinical event and positive laboratory test

“Non-criteria” APS findings

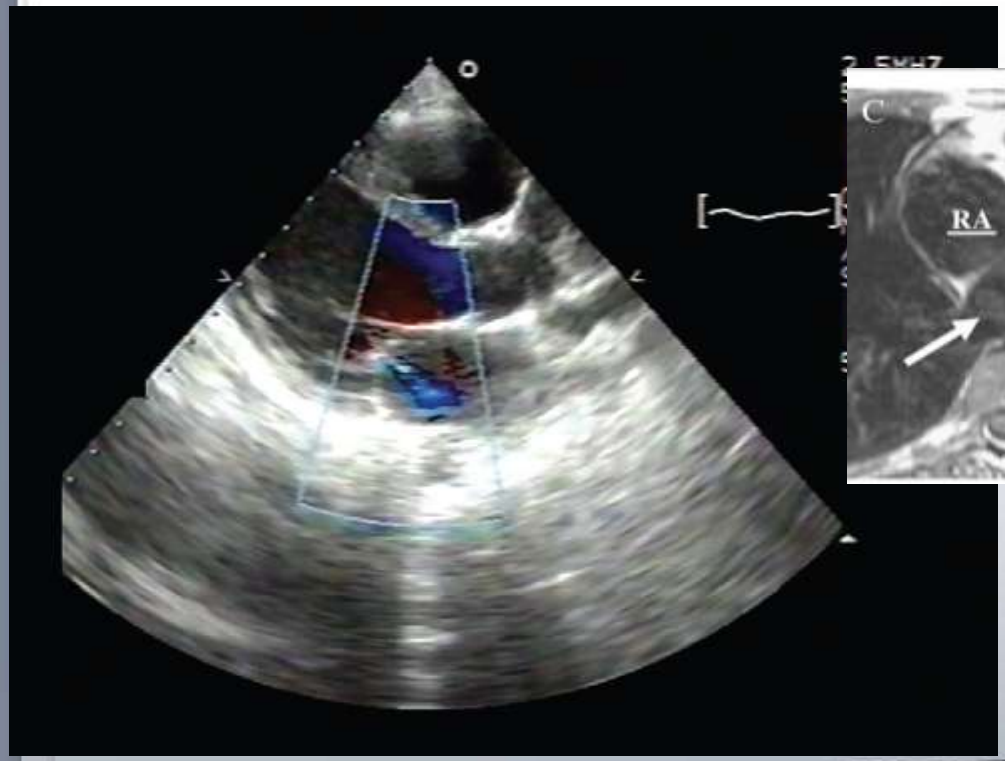
- Thrombocytopenia and/or hemolytic anemia.
- Transverse myelopathy or myelitis.
- Avscular necrosis of the hip.

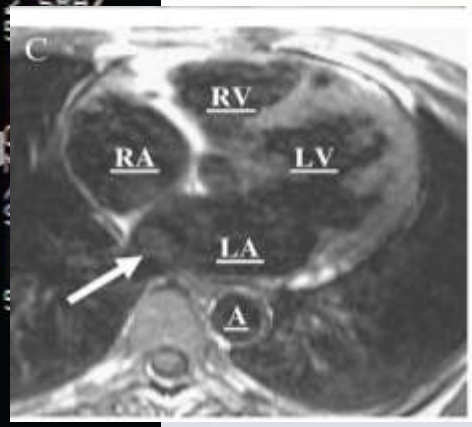
-- Miyakis, *et al*., J.Thromb.Haemost., 2006; 4: 295

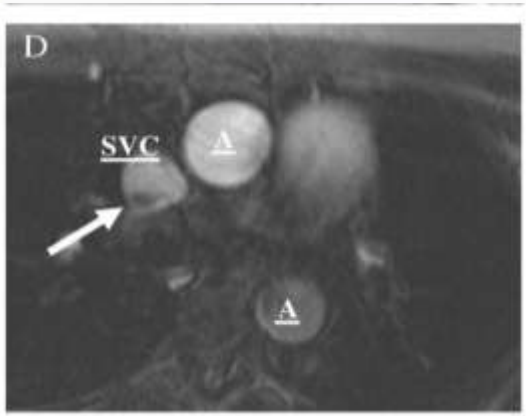
Livido reticularis.



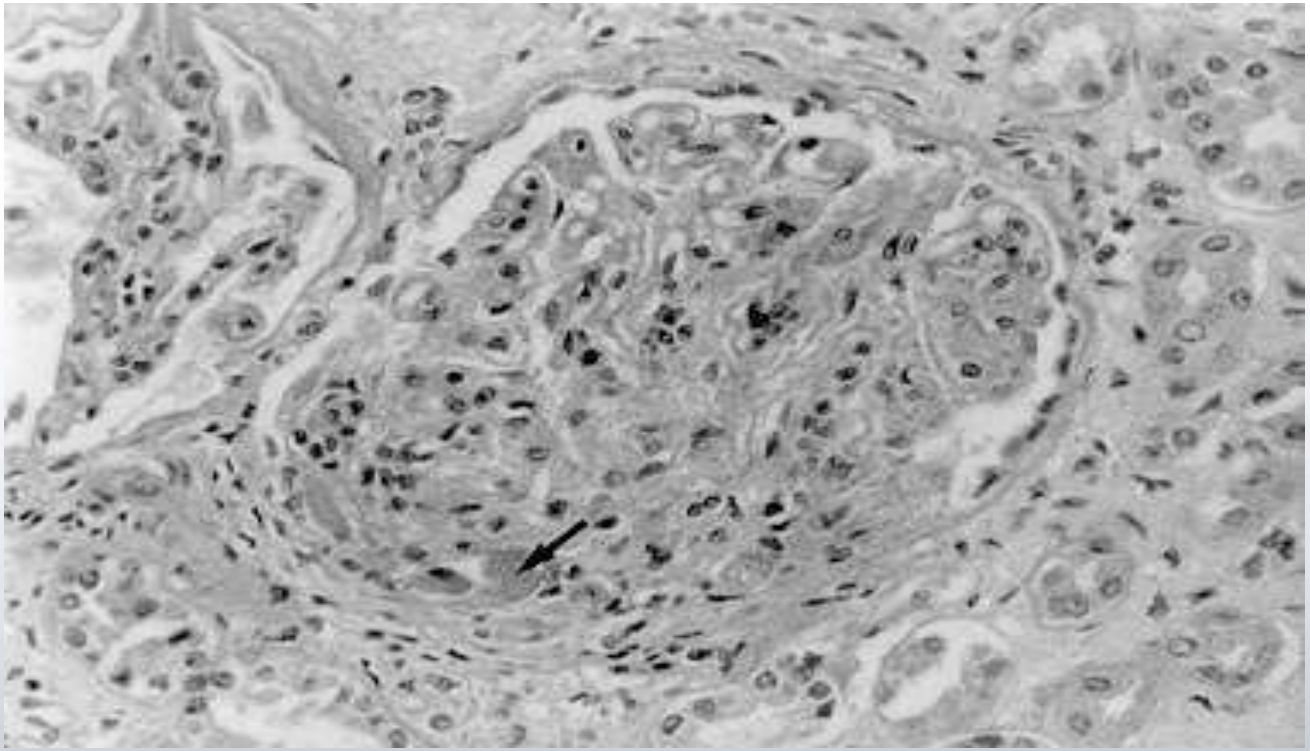
Cardiac valve disease.







nephropathy

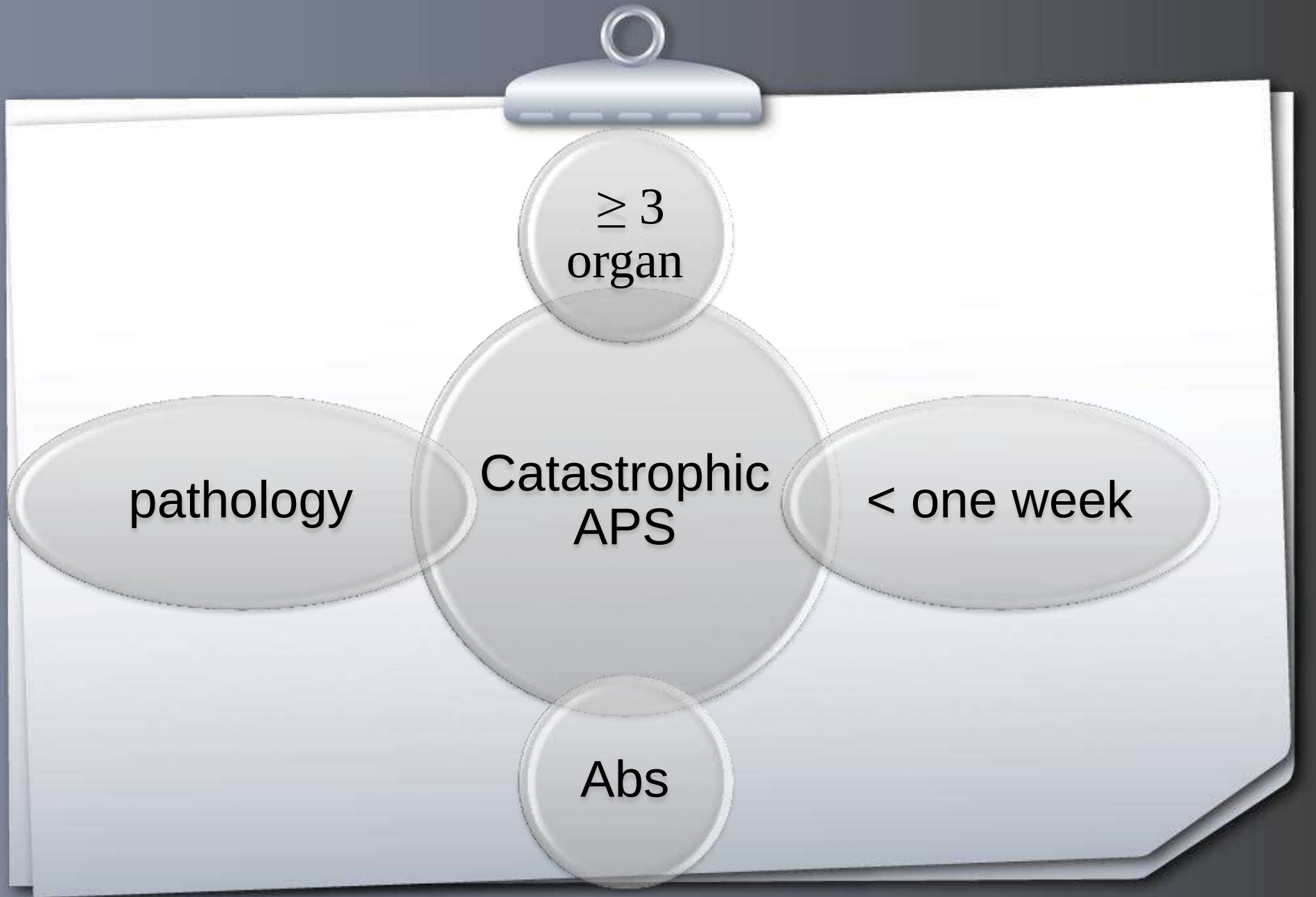


Focal glomerular microthrombosis

Non-thrombotic neurologic manifestations……

multiple sclerosis-like syndrome,

chorea, or migraine headaches


≥ 3 organ
pathology
Catastrophic APS
< one week
Abs

Investigations

Anti-Phospholipid antibodies

- Lupus Anti-coagulant (more specific, less sensitive)
- Anti-cardiolipin antibody(IgG, IgM, IgA)
- Anti-ß2 glycoprotein I antibody (IgG, IgM, IgA)
- Anti-prothrombin
- Anti annexin V
- False + serologic test for Syphillis

- ANA, Anti ds DNA
- Thrombocytopenia (usually >50,000)
- Proteinuria and renal insufficiency
- ESR, Hb,WBC
- MRI, MRA, echo,
- patholgy

if feasible…….advisable

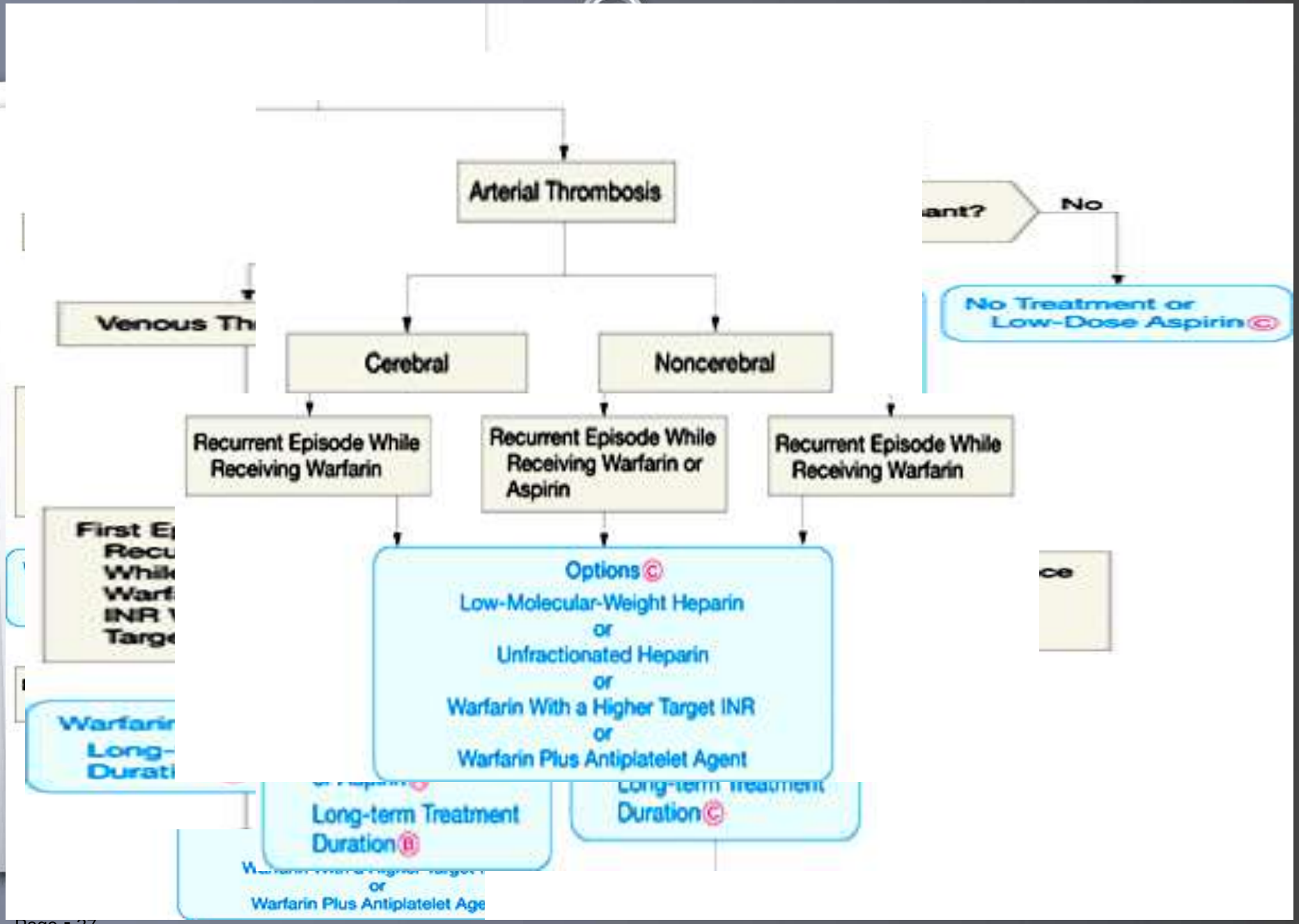
- Protein C, S
- Antithrombin III
- Factor V leiden
- Prothrombin mutations
- hyperhomocysteinemia

treatment

- **Asymptomatic - no treatment (?ASA)**
- **anticoagulation**
  - **Heparin**
  - **Warfarin**

    (INR 2-3)
- **Pregnancy – controversial**
  - **?? treat with ASA + heparin even without history of thrombosis**

- Risk factor modification (smoking , OCP)
- HQL, antiplatelet
- Treat associated condition eg.SLE
- Immunosuppresion – rarely used
- Plasmapharesis
- IVIG
- Novel therapies



Lim, W. et al. JAMA 2006;295:1050-1057.

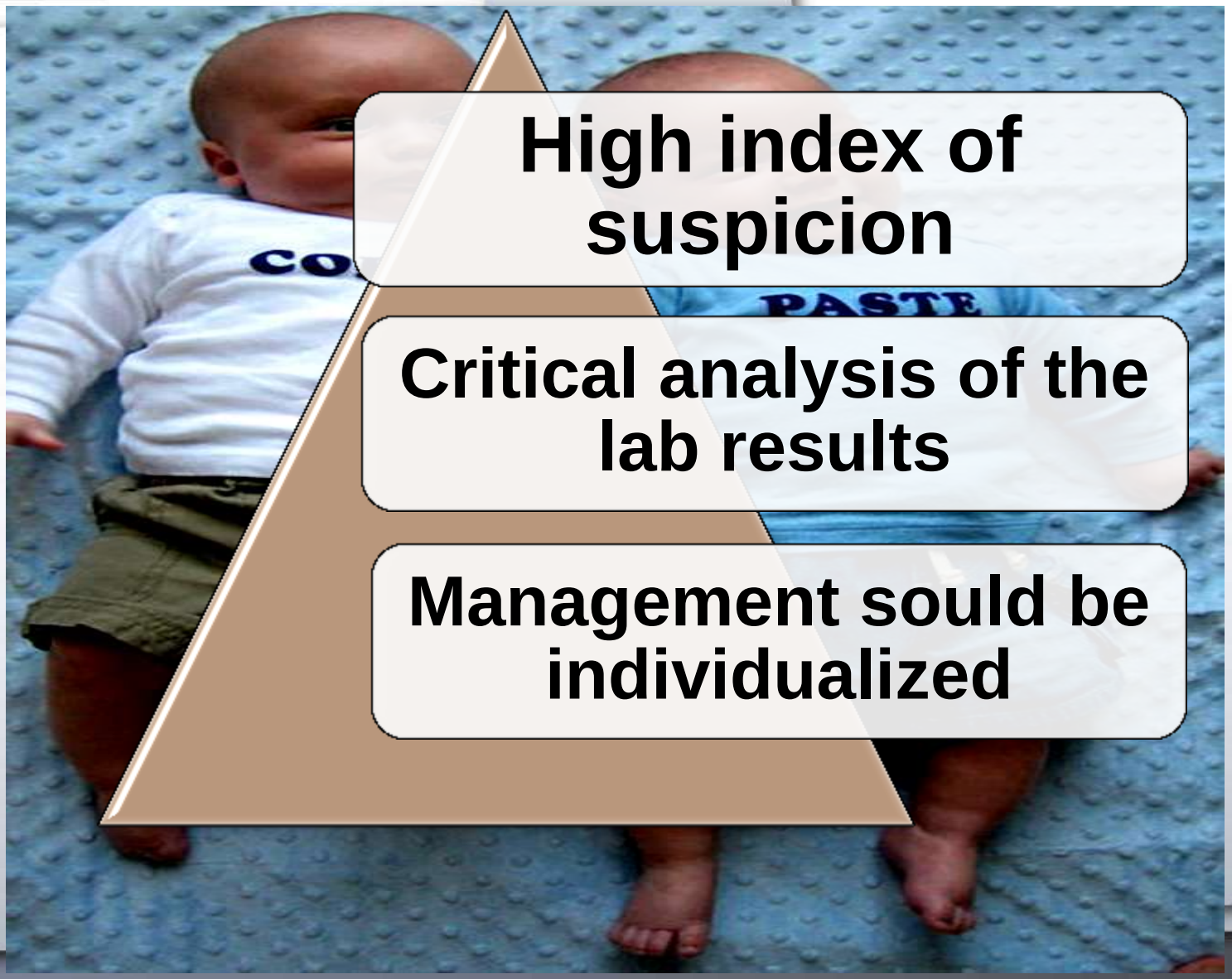
Future directions

- Peptide-specific therapy: B2GPI blocking Ab
- Inhibitors of intracellular signaling triggered by aPL
- Complement activation inhibitors
- IL3, statins
- Anti-TNFα agents
- Anti CD20 agents

Treatment - CAPS

- Anticoagulation
- Steroids
- Plasmapharesis or IVIG
- Treatment of any precipitant eg. Infection
- Cytotoxics (if indicated eg.Active SLE)
- Anti CD 20

Conclusion


High index of suspicion
Critical analysis of the lab results
Management sould be individualized

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Thank you